

十一、研究計畫中英文摘要：請就本計畫要點作一概述，並依本計畫性質自訂
關鍵詞。

(二) 計畫英文摘要。(五百字以內)

Angiogenesis is required to sustain primary tumor enlargement as well as metastasis. The induction of tumor angiogenesis is mediated by the increased production of various angiogenic molecules released by tumor cells, including vascular endothelial growth factor (VEGF), matrix metalloproteinases (MMPs) and cytokine. Among the angiogenic factors, VEGF was found to be the most potent. The expression of VEGF has been shown to be markedly associated with the secretion of cytokine, such as interleukin,(IL)-12, interferon (IFN) and tumor necrosis factor (TNF)- α by the immune system.

Epidemiologic studies have shown that high lycopene intakes are associated with low risk of several types of cancer. Lycopene is known to possess antioxidant, immunomodulatory and anticancer activities, especially prostate cancer, and is an important topic of anticancer research. It should be noted that the immuno-regulatory action is related with anti-angiogenesis. However, it is unclear whether lycopene can inhibit angiogenesis via immunomodulatory action.

We have identified several important issues in review of the literature. We intend to study two major issues that we are able to tackle and resolve. One issue is whether lycopene can inhibit angiogenesis and how they exert these effects. We recently showed that lycopene mediated angiogenic factors, including the inhibition of VEGF and MMPs and up-regulation of IL-12 secretion in nude mice (Huang et al., *J. Nutr.* 2008). However, the anti-angiogenic effects and mechanisms of action of lycopene have not been reported. Another issue is the possible mechanism about immunomodulation. To examine the following issues, we intend to use the human umbilical vein endothelial cell lines (HUVEC) as *in vitro* angiogenesis model.

- 1) In the first year, we will evaluate the immunomodulatory effects of lycopene by analyzing the production of cytokines in mononuclear cells stimulated with lycopene in order to provide insights into the immune function that controls angiogenesis in response to lycopene.
- 2) In the second year, we will investigate the anti-angiogenic effect of lycopene in an *ex-vivo* model, closely mimicking physiological conditions. Gerbils will be supplemented with lycopene orally, and their serum used in *in vitro* studies on angiogenesis of HUVEC, and the immunomodulatory mechanism.
- 3) In the third year, we will investigate the *in ex-vivo* and *in vivo* anti-angiogenic effects of lycopene and the mechanisms.

This research project is expected to increase our knowledge of the anti-angiogenic effects and immunomodulatory mechanism of lycopene. In addition,

these studies can not only promote the level of basic research in Taiwan, but also contributes directly or indirectly to the health of people worldwide.

Keywords: lycopene, immunomodulation, anti-angiogenesis, cytokine